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GE HEALTHCARE BIO-SCIENCES CORP.
PATENT DEPARTMENT
101 CARNEGIE CENTER
PRINCETON, NJ 08540

EXAMINER	
DIETERLE, JENNIFER M	

ART UNIT	PAPER NUMBER
1795	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

melissa.leck@ge.com

Office Action Summary	Application No.	Applicant(s)	
	10/523,304	CONLEY, EDWARD C.	
	Examiner	Art Unit	
	Jennifer Dieterle	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/24/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-20 are being addressed.

Response to Amendment

1. Applicant's amendment of 11/24/2009 does not render the application allowable. In light of applicant's remarks, the prior rejection is maintained; however, a non-final has been issued since claim 10 was not addressed. Claim 10 has been addressed below. Additionally, upon further consideration, a new ground(s) of rejection is made in view of Dineen et al. (US 7,101,472 B2, provisional 60/364,213 filed on March 13, 2002), Norwood et al. (WO 01/071349 A1) or Noboru (JP 11299496) in view of Hewson et al. (US 4,960,133).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 12 and 13 recite the limitation "reference electrode". There is insufficient antecedent basis for this limitation in the claim.

Specification

3. The amendment filed 11/24/09, same claims as filed 5/26/09, is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35

U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Claim 19 refers to an electrode needle that has a cavity configured to receive a sensing electrode. It is not clear from where this new matter is derived from in applicant's specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Dineen et al. (US 7,101,472 B2, provisional 60/364,213, files March 13, 2002, citing to the US Patent Document).

Regarding claim 1, Dineen et al. teach a device comprising (see col. 4):

- A hollow sheath (figure 1, number 106);
- The sheath is open at the tip (figure 1, 133); and

- The sheath surrounding an electrode (figure 1, number 109) having a plurality of sensing areas (figure 1, 115).

With respect to electrode arrangement being capable of cell holding, the term “cell holding" merely specify the intended use of the electrode arrangement and does not infer any structural distinction to the device. This limitation does not further define the structure of the electrode arrangement, but only specify how the electrode arrangement is intended to interface with the sample. Hence, these limitations do not further define the actual structure of the sensor, but merely set forth the intended use of the sensor. Intended use need not be given further due consideration in determining patentability of an apparatus.

Regarding claim 2, Dineen et al. teach that the electrode does not extend beyond the tip of the sheath (see figure 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being obvious over Dineen et al. (US 7,101,472 B2, provisional 60/364,213, files March 13, 2002, citing to the US Patent Document) in view of Lee et al. (US 4,128,456)

Regarding claim 1, Dineen et al. teach a device comprising (see col. 4):

- A hollow sheath (figure 1, number 106);
- The sheath is open at the tip (figure 1, 133); and
- The sheath surrounding an electrode (figure 1, number 109) having a plurality of sensing areas (figure 1, 115).

If patentable weight is given with respect to electrode arrangement being capable of cell holding, Lee et al. teach the use of a hollow sheath that can be evacuated to hold a cell at its tip (abstract; figure 2; #10 body and #52 suction pipette that holds wire) that is capable of holding a puncture wire 28 (col. 3; lines 4-10). The hollow sheath has a cell holding end 56 in which a captured cell is held by a vacuum and allows the wire to be inserted into the cell in order to perform electrical measurements. The suction sheath holds the cell firmly minimizing movement and vibration which allows for good electrical contact and allows for continuous and rapid response for the recording of

intracellular activity. The configuration allows for the changing of the environment of the cell under study and is small easy to use and maintain (col. 2; lines 1-12 and 37-48). The hollow sheath also mechanically supports the wire (col. 2; lines 10-12).

Therefore, it would have been obvious to one skilled in the art to modify the sheath of Dineen et al. to hold an individual cell as the device taught by Lee et al. because the analysis of an individual cell will require less sample volume.

Regarding claim 2, Dineen et al. teach that the electrode does not extend beyond the tip of the sheath (see figure 1).

6. Claims 1-3, 5, 7-9, 14, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al. (U.S. 6,135,990) in view of Lee et al. (U.S. 4,128,456).

Regarding claims 1, 7, 14 and 20, Heller et al. teach an electrode arrangement and method of use comprising elongated needles (col. 5, lines 60-64) with a plurality of sensing electrodes (see figure 4; #13, 14, 15 are electrodes; col. 5; lines 38-67; col. 6; lines 7-14).

Heller et al. do not teach the use of a hollow sheath open at a cell-contact tip that surrounds at least one electrode needle.

Lee et al. teach the use of a hollow sheath that can be evacuated to hold a cell at its tip (abstract; figure 2; #10 body and #52 suction pipette that holds wire) that is capable of holding a puncture wire 28 (col. 3; lines 4-10). The hollow sheath has a cell

holding end 56 in which a captured cell is held by a vacuum and allows the wire to be inserted into the cell in order to perform electrical measurements. The suction sheath holds the cell firmly minimizing movement and vibration which allows for good electrical contact and allows for continuous and rapid response for the recording of intracellular activity. The configuration allows for the changing of the environment of the cell under study and is small easy to use and maintain (col. 2; lines 1-12 and 37-48). The hollow sheath also mechanically supports the wire (col. 2; lines 10-12).

Therefore, it would have been obvious to one skilled in the art to modify the needles of Heller et al. to include hollow sheath covers as taught by Lee et al. because the hollow sheath will provide support for each needle (Lee et al. col. 2; lines 34-38).

Additionally, it would have been obvious to one skilled in the art to modify the device of Heller et al. because the device of Heller et al. exposes the cells or tissue to a drug or molecule and then uses electrical current for electroportation (col. 3; lines 24-35). By modifying the needles of Heller et al. by placing a hollow cell holding sheath around the needle as taught by Lee et al. would allow for the device of Heller et al. to place the drug or molecule directly into the cells of interest and circumvent the step of electroportation because it would allow for the holding of a cell and the direct placement of the drug or molecule inside the cell of interest (Lee et al. col. 3; lines 4-10).

Regarding claim 2, Heller et al., in view of Lee et al. as stated above in claim 1, teach an electrode arrangement with an electrode needle containing a plurality of electrodes.

Lee et al. teach that the puncture wire 28 is inserted in the captured cell for electrical measurement (col. 3, lines 45-46) and since the captured cell is "suctioned" onto the sheath it is inherent that part of the cell will be inside the sheath and that the puncture wire will extend only to the tip of the sheath based on the amount of suction and how far the cell extends into the sheath.

The court held that adjustability, where needed, is not a patentable advance. See *In re Stevens*, 212 F.2d 197, 101 USPQ 284 (CCPA 1954)(MPEP 2144V D). Therefore, it would have been obvious to one skilled in the art to modify the device of Heller et al. to have the electrode needle extend only to the end of the hollow sheath.

Regarding claims 3 and 9, Heller et al., in view of Lee et al. as stated above in claim 1, teach a cell holding device in which a vacuum is applied in order to prevent cell-removal (col. 1, line 68).

Regarding claim 5, Heller et al., in view of Lee et al. as stated above in claim 1, teach a device that is capable of removing a cell from a cell cluster mechanically (Lee et al. col. 1, line 68 and col. 2, line 1). Therefore, it would be obvious to one skilled in the art that the cell cluster would be held in a well type device prior to separation. The device would be inserted into the well device in order to perform the separation.

Regarding claim 8, Heller et al., in view of Lee et al. as stated above in claim 1, teach a cell holding device in which a vacuum is applied in order to prevent cell-removal

(col. 1, line 68). It is well know in the art that suction is the flow of a fluid into a partial vacuum or region of low pressure. The pressure gradient between this region and the ambient pressure will propel matter toward the low pressure area. Therefore, a vacuum does not innately attract matter, it is actually being pushed in by the higher pressure air on the outside. With regard to claim 8, the method of pushing a cell onto the electrode is the same as applying a vacuum as taught by Heller et al. in view of Lee et al. (Lee et al. col. 1, line 68) in that a vacuum actually operates as to "push" the cell onto the sheath.

Regarding claim 19, Heller et al., in view of Lee et al. as stated above in claim 1, teach an electrode needle 12 comprising a cavity formed there in which there are multiple electrodes 13, 14, 15 (see Heller et al. figure 4).

7. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al. (U.S. 6,135,990) and Lee et al. (U.S. 4,128,456) in further view of Tachibana et al. (U.S. Pat. No. 6,096,000).

Regarding claim 4, Heller et al., in view of Lee et al., teach a intracellular potential measurement device comprising a hollow sheath with a multiple electrodes, but does not teach the use of a non-ion-conducting sealing compound.

Tachibana et al. teach the use of a non-ion-conducting sealant such as petroleum jelly between the housing and tissue to prevent leakage (col. 4, lines 19-21).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Heller et al. by using a non-ion-conducting sealant on the needle as taught by Tachibana et al., to provide a better seal to prevent leakage between the cell and measuring device (Tachibana et al. col. 4, lines 19-21).

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8. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al. (U.S. 6,135,990) and Lee et al. (U.S. 4,128,456) in further view of Schroeder et al. (U.S. 7,270,730 B2).

Regarding claim 6, Heller et al. in view of Lee et al. as stated above in claim 1, teach a potential measurement device comprising a hollow sheath with a plurality of electrodes, but does not teach the use of a automated manipulating device.

Schroeder et al. teach an automated system to perform electrophysiological measurements on a plurality of samples simultaneously comprising an electronics head having a plurality of electrodes (figure 6, #84 and 86; col. 11, lines 43-60). This automated device allows for motion control, fluidics control, and electrical data recording.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Heller et al. by placing it onto an automated device as taught by Schroeder et al. in order to perform testing on a plurality of samples simultaneously (Schroeder et al. col. 11, lines 43-60).

9. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al. (U.S. 6,135,990) and Lee et al. (U.S. 4,128,456) in view of Vestergaard et al. (US 2004/005696, provisional 60/372796 filed April 17, 2002, citing to PG Pub).

Regarding claim 10, Heller et al. teach an electrode arrangement for holding cells, but does not specifically teach applying suction based on cells predetermined conductivity.

Vestergaard et al. teach a cell holding device that in which an electric field from an electrode draws the charged cell towards it or negatively charged cells will be drawn towards positive electrodes and vice versa (i.e. changing the conductivity of the cell). The electrostatic pull can also act as guiding means (paragraph [0079]). In order to draw the cell to the tip of the pipette, as well as to make the necessary contact for obtaining the gigaseal, it is normal to apply suction to the pipette (paragraph [0078]). Alternatively, the positioning of a cell over an aperture in the substrate can be carried out by electro-osmosis (paragraph [0080].

Therefore, it would have been obvious to one skilled in the art to modify the attachment method of Heller et al. to use suction based on a predetermined conductivity measurement as taught by Vestergaard et al. because applying suction forms a gigaseal for effective cell holding.

10. Claims 11-13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al. (U.S. 6,135,990) and Lee et al. (U.S. 4,128,456) in further view of Rubinsky et al. (US 2001/0046706 A1).

Regarding claims 11-13, 17 and 18, Heller et al., in view of Lee et al. as stated above in claim 1, teach a potential measurement device comprising a hollow sheath with a plurality of electrodes, but does not teach: identifying the change in conductivity between the cell and the electrodes; positioning the cell based on this change; and creating a vacuum within the sheath based on this change.

Rubinsky et al. teach the use of impedance (i.e. conductivity) to determine the location of a cell using two electrodes (see figure 2, #27 and 26).

Therefore, it would have been obvious to try to use the conductivity change between the cell and the electrodes located in the needle of Heller et al. to determine whether the cell is located over the hollow sheath in order to determine the precise time at which to provide suction to the hollow sheath since the suction is only effective when a cell is under the sheath. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1395-97 (2007) (MPEP 2143 E).

11. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al. (U.S. 6,135,990) and Lee et al. (U.S. 4,128,456) in view of Walker et al. (US 2004/0127776 A1).

Regarding claim 15, Heller et al. teach a cell holding arrangements, but do not specifically teach a barbed device to retain a cell.

Walker et al. teach that barbs can be placed on needles to hold an object in place (see figure 5).

Therefore, it would be obvious to one skilled in the art to modify the needle of Heller et al. to include a barb as taught by Walker et al. because a barb will provide an additional means for holding a cell onto a needle.

Additionally, regarding claim 15, barbs on wires and tapered rings are all old and well known expedients in the art and represent well known ways in which to hold an object onto a device. (See *In re Zurko*, 258 F.3d 1379, 1385, 59 USPQ2d 1693, 1697 (Fed. Cir. 2001); *Ahlert*, 424 F.2d at 1092, 165 USPQ at 421; MPEP 2144.03A).

12. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al. (U.S. 6,135,990) and Lee et al. (U.S. 4,128,456) in view of Quijano et al. (US 5,824,061).

Regarding claim 16, Heller et al. teach a cell holding arrangements, but do not specifically teach a tapered ring to retain a cell.

Quijano et al. teach the use of tapered rings as a means for holding/securing (see figures 5-8).

Therefore, it would be obvious to one skilled in the art to modify the needle of Heller et al. to include a tapered ring as taught by Quijano et al. because a tapered ring will provide an additional means for holding a cell onto a needle.

Additionally, regarding claim 16, barbs on wires and tapered rings are all old and well known expedients in the art and represent well known ways in which to hold an

object onto a device. (See *In re Zurko*, 258 F.3d 1379, 1385, 59 USPQ2d 1693, 1697 (Fed. Cir. 2001); *Ahlert*, 424 F.2d at 1092, 165 USPQ at 421; MPEP 2144.03A).

REJECTION UTILIZING NORWOOD OR NOBORU:

13. Claims 1-3, 5-7, 14, 19 and 20 are rejected under 35 U.S.C. 103(a) as being obvious over Norwood et al. (WO 01/071349 A1) or Noboru (JP 11299496) in view of Hewson et al. (US 4,960,133).

Regarding claims 1, 14, 19 and 20, Norwood et al. teach a patch clamp (i.e. cell holding) arrangement comprising a glass pipette (i.e. electrode sheath) whereby cells are attached to form an electrical seal (i.e. sheath is open at a cell contact tip) and the pipette contains an Ag/AgCl wire (i.e. electrode needle) (abstract, pages 2-5, figures 5a-b).

Norwood et al. do not teach that the Ag/AgCl wire (i.e. electrode needle) contains a plurality of sensing electrodes.

Noboru teaches a patch clamp (i.e. cell holding) arrangement comprising a conical vessel (i.e. electrode sheath) whereby cells are attached to form an electrical seal (i.e. sheath is open at a cell contact tip) and the vessel contains an electrode (i.e. electrode needle) (abstract, section [0011-13], figures 1A-B).

Noboru does not teach that the electrode (i.e. electrode needle) contains a plurality of sensing electrodes.

It is noted that applicant's at section 0014 of their specification describe the electrode needle as being provided with a plurality of sensing electrodes which are in the form of ring electrodes, preferably mounted flush with the surface of electrode needle with the longitudinal axes of the ring electrodes concentric with the longitudinal axis of the electrode needle.

Hewson et al. teach a catheter device that comprises at least one wire (i.e. electrode needle) surrounded by a sheath that contains a plurality of ring electrodes around the wire. The wire rings provide maximum electrical contact surfaces (col. 3-4). The device can measure the resistance or impedance between the rings or provide a pulse of energy (col. 4-5).

Applicant's specification does not provide for the specific function of the sensing electrodes. Since it is known that patch clamp techniques utilize an electrode to sense an electrical property of a cell (Norwood et al. or Noboru), and it is known in the art to provide multiple ring electrodes on a wire as taught by Hewson et al.; therefore, it would have been obvious to one skilled in the art to modify the wire/electrode in Norwood et al. or Noboru to include multiple ring electrodes as taught by Hewson et al. because ring electrodes provide maximum electrical contact surfaces and allow for multiple electrical measurements such as resistance or impedance between the rings or provide a pulse of energy thereby adding additional functionality known in the art to the wire/electrode of Norwood et al or Noboru.

With regard to claim 14, the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. In re Harza,

274 F.2d 669, 124 USPQ 378 (CCPA 1960); MPEP 2144.04 VI B. In the given application, no reference is provided in applicant's specification of any new of unexpected results by providing a plurality of electrode needles in each sheath. Given, as discussed above, that electrical properties of cells are measured utilizing a electrode needle that can be modified with a plurality of ring electrodes, providing multiple electrode needles (i.e. duplication of parts) has no patentable significance without new or unexpected results. Therefore, it would have been obvious to one skilled in the art to modify the device of Norwood et al. or Noboru to include multiple needle electrodes because the act of duplicating parts without any new results (i.e. electrical properties will still be measured in a cell).

With regard to claim 20, both Norwood et al. and Noboru teach the use of a sheath containing an electrode needle. The court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. In re Harza, 274 F.2d 669, 124 USPQ 378 (CCPA 1960); MPEP 2144.04 VI B. Since sheaths are known in the art to provide support, and given, as discussed above, that a sheath is provided to surround the electrode needle, providing additional sheaths (i.e. duplication of parts) has no patentable significance without new or unexpected results. Therefore, it would have been obvious to one skilled in the art to modify the device of Norwood et al. or Noboru to include multiple layers of sheaths because the act of duplicating parts without any new results (i.e. electrical properties will still be measured in a cell).

Regarding claim 2, both Norwood et al. (figure 5b) and Noboru (figure 1B) teach that the electrode does not extend beyond the tip of the sheath.

Regarding claim 3, both Norwood et al. and Noboru teach that the electrode is provided with a cell-removal preventing device. Norwood et al. teach the formation of a G-seal (page 6). Noboru teaches the use of a fixing container and gravity (section 0013-15).

Regarding claim 5, Norwood et al. (figure 1, pages 13-14) teach that the sheath can be arranged inside a well and Noboru (figure 7) teach that the sheath can be arranged so as to have a sample solution flow over it which can be construed as a "well".

Regarding claim 6, Norwood et al. teach that the sheath can be connected to a mechanical manipulator to bring respective parts of the patch clamp into close proximity (page 11) and Noboru teaches that a driving force can be utilized to move the patch clamp (section 0020-224).

Regarding claim 7, Noboru teaches a patch clamp (i.e. cell holding) arrangement comprising a conical vessel (i.e. electrode sheath) whereby cells are attached to form an electrical seal (i.e. sheath is open at a cell contact tip) and the vessel contains an

electrode (i.e. electrode needle) (abstract, section [0011-13], figures 1A-B). Noboru (section 0019, figure 4) teach penetrating a cell.

Noboru does not teach that the electrode (i.e. electrode needle) contains a plurality of sensing electrodes.

It is noted that applicant's at section 0014 of their specification describe the electrode needle as being provided with a plurality of sensing electrodes which are in the form of ring electrodes, preferably mounted flush with the surface of electrode needle with the longitudinal axes of the ring electrodes concentric with the longitudinal axis of the electrode needle.

Hewson et al. teach a catheter device that comprises at least one wire (i.e. electrode needle) surrounded by a sheath that contains a plurality of ring electrodes around the wire. The wire rings provide maximum electrical contact surfaces (col. 3-4). The device can measure the resistance or impedance between the rings or provide a pulse of energy (col. 4-5).

Applicant's specification does not provide for the specific function of the sensing electrodes. Since it is known that patch clamp techniques utilize an electrode to sense an electrical property of a cell Noboru, and it is known in the art to provide multiple ring electrodes on a wire as taught by Hewson et al.; therefore, it would have been obvious to one skilled in the art to modify the wire/electrode in Noboru to include multiple ring electrodes as taught by Hewson et al. because ring electrodes provide maximum electrical contact surfaces and allow for multiple electrical measurements such as

resistance or impedance between the rings or provide a pulse of energy thereby adding additional functionality known in the art to the wire/electrode of Noboru.

14. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Norwood et al. (WO 01/071349 A1) or Noboru (JP 11299496) and Hewson et al. (US 4,960,133), in further view of Tachibana et al. (U.S. Pat. No. 6,096,000).

Regarding claim 4, Norwood et al. and Noboru, in view of Hewson et al., teach an intracellular potential measurement device comprising a hollow sheath with a needle and multiple ring electrodes (i.e. sensing electrodes), but does not teach the use of a non-ion-conducting sealing compound.

Tachibana et al. teach the use of a non-ion-conducting sealant such as petroleum jelly between the housing and tissue to prevent leakage (col. 4, lines 19-21).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Norwood et al. or Noboru by using a non-ion-conducting sealant on the needle as taught by Tachibana et al., to provide a better seal to prevent leakage between the cell and measuring device (Tachibana et al. col. 4, lines 19-21).

15. Claim 8-11 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noboru (JP 11299496) and Hewson et al. (US 4,960,133) in view of Norwood et al. (WO 01/071349 A1).

Regarding claims 8-11 and 17, Noboru teaches a cell holding device, but does not teach the use of suction, based on a predetermined conductivity measurement, to pull the cell onto the electrode.

Norwood et al. teach a cell holding device in which suction based on established based on predetermined resistance between pipette and cell suspension is utilized when suspension falls into the region of 200M to 3G (page 16).

Therefore, it would have been obvious to one skilled in the art to modify the way in which is cell is held onto the patch clamp in Noboru by providing a vacuum (i.e. suction) to prevent cell removal the suction being based on a predetermined resistance between pipette and cell suspension as taught by Norwood et al. because suction will act to prevent cell removal and since suction is the flow of a fluid into a partial vacuum or region of low pressure and the pressure gradient between this region and the ambient pressure will propel matter toward the low pressure area. Therefore, a vacuum does not innately attract matter, it is actually being pushed in by the higher pressure air on the outside. With regard to claim 8, the method of pushing a cell onto the electrode is the same as applying a vacuum (i.e. pull) in that a vacuum actually operates as to "push" the cell onto the sheath.

16. Claim 12, 13 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noboru (JP 11299496) and Hewson et al. (US 4,960,133) in view of Oka et al. (US 2003/0113833 A1; WO 02/055653 A1, citing is to the US document).

Regarding claims 12, 13 and 18, Noboru teaches a cell holding device, but does not teach a reference electrode used to detect a change in conductivity and then apply suction based on the change.

Oka et al. teach an extracellular potential measuring device capable of simply and highly reliably detecting a change in a minute electrical signal emitted by a biological sample. Oka et al. teach the device comprises at least one well comprising means for holding a cell provided on a substrate, a measuring electrode for detecting an electrical signal of each of the at least one well, and a reference electrode. The cell holding means comprises at least one depression provided within the well, and has a throughhole at a bottom surface thereof, the throughhole being linked to means for suctioning the cell (abstract) to measure electrical current.

Therefore, it would have been obvious to one skilled in the art to modify the device of Noboru to include a reference electrode as taught by Oka et al. because a reference electrode will allow for the measurement of an electrical signal.

17. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Norwood et al. (WO 01/071349 A1) or Noboru (JP 11299496) and Hewson et al. (US 4,960,133) in view of Walker et al. (US 2004/0127776 A1)

Regarding claim 15, both Norwood et al. and Noboru teach a cell holding arrangements, but do not specifically teach a barbed device to retain a cell.

Walker et al. teach that barbs can be placed on needles to hold an object in place (see figure 5).

Therefore, it would be obvious to one skilled in the art to modify the needle of Norwood et al. or Noboru to include a barb as taught by Walker et al. because a barb will provide an additional means for holding a cell onto a needle.

Additionally, regarding claim 15, barbs on wires and tapered rings are all old and well known expedients in the art and represent well known ways in which to hold an object onto a device. (See *In re Zurko*, 258 F.3d 1379, 1385, 59 USPQ2d 1693, 1697 (Fed. Cir. 2001); *Ahlert*, 424 F.2d at 1092, 165 USPQ at 421; MPEP 2144.03A).

18. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Norwood et al. (WO 01/071349 A1) or Noboru (JP 11299496) and Hewson et al. (US 4,960,133) in view of Quijano et al. (US 5,824,061).

Regarding claim 16, both Norwood et al. and Noboru teach a cell holding arrangements, but do not specifically teach a tapered ring to retain a cell.

Quijano et al. teach the use of tapered rings as a means for holding/securing (see figures 5-8).

Therefore, it would be obvious to one skilled in the art to modify the needle of Norwood et al. or Noboru to include a tapered ring as taught by Quijano et al. because a tapered ring will provide an additional means for holding a cell onto a needle.

Additionally, regarding claim 16, barbs on wires and tapered rings are all old and well known expedients in the art and represent well known ways in which to hold an object onto a device. (See *In re Zurko*, 258 F.3d 1379, 1385, 59 USPQ2d 1693, 1697 (Fed. Cir. 2001); *Ahlert*, 424 F.2d at 1092, 165 USPQ at 421; MPEP 2144.03A).

Response to Arguments

Applicant's arguments filed 11/24/09, with respect to claims 1-20 have been fully considered and are not persuasive.

19. Applicant's remark that no person skilled in the art would consider using the needle of Heller et al. to penetrate individual cells. However, as noted in office action dated 8/31/09, Heller et al. exposes the cells or tissue to a drug or molecule and then uses electrical current for electroportation (col. 3; lines 24-35). By modifying the needles of Heller et al. by placing a hollow cell holding sheath around the needle as taught by Lee et al. would allow for the device of Heller et al. to place the drug or molecule directly into the cells of interest and circumvent the step of electroportation because it would allow for the holding of a cell and the direct placement of the drug or molecule inside the cell of interest (Lee et al. col. 3; lines 4-10).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dieterle whose telephone number is (571) 270-7872. The examiner can normally be reached on Monday thru Friday, 8am to 5pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alexa Neckel can be reached on (571) 272-1446. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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JMD
3/29/10

/Alexa D. Neckel/

Supervisory Patent Examiner, Art Unit 1795